Student Paper Communication étudiante

Uveal amelanotic melanoma in a ragdoll cat

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Abstract — A 13-year-old castrated male ragdoll cat's left eye was evaluated for dyscoria, iridal thickening and color change of 2 years duration, as well as elevated intraocular pressure. The primary lesion seen on ophthalmic examination was a pale pink-white mass observed in the dorsomedial aspect of a diffusely thickened iris. Metastatic workup revealed hepatic and splenic nodules, but cytology was inconclusive. The left eye was enucleated, and histopathology was consistent with uveal amelanotic melanoma.

Résumé — Mélanome uvéal amélanotique chez un chat ragdoll. L'œil gauche d'un chat mâle ragdoll castré âgé de 13 ans fut évalué pour dyscorie, épaississement iridien et changement de couleur présent depuis deux ans, de même que pour une pression intra-oculaire élevée. La lésion primaire vue lors de l'examen ophtalmique était une masse blanc-rosée pâle observée à l'aspect dorso-médial d'un iris épaissi de manière diffuse. Une vérification pour métastases révéla des nodules hépatiques et spléniques, mais la cytologie était non-concluante. L'œil gauche fut énucléé et l'histopathologie était compatible avec un mélanome uvéal amélanotique.

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A 13-year-old castrated male ragdoll cat was presented to the ophthalmology service of the Ontario Veterinary College Health Sciences Centre (OVC-HSC) for evaluation of iris color change and elevated intraocular pressure in the left eye. Approximately 2 years earlier, the left iris had changed in color from blue to yellow. One week before presentation, the iris began to bulge toward the pupil resulting in dyscoria. At that time, the intraocular pressure (IOP) in the left eye was elevated (26 mmHg; normal mean IOP: 18.4 +/− 0.5 mmHg) based on applanation tonometry (Tono-Pen Vet; Veterinary Tonometer: Reichert, Buffalo, New York, USA) (1). A tentative diagnosis of uveitis with secondary glaucoma was made by the referring veterinarian, and the patient was started on topical dorzolamide 2% (Trusopt; McKesson, Brampton, Ontario), 1 drop oculus sinister (OS) (left eye), q8h and topical prednisolone acetate 1% (Sandoz Prednisolone; Sandoz, Boucherville, Quebec), 1 drop OS q8h. There was no known history of ocular trauma or infectious systemic disease. Previously diagnosed medical conditions included feline asthma, intermittent episodes of constipation, and impaired left ventricular diastolic function.

On admission, the patient was bright, alert, and responsive, with vital parameters within normal limits. A grade III/VI left systolic heart murmur was auscultated, with strong synchronous femoral pulses. The remainder of the physical examination was unremarkable.

On ophthalmic examination, the dazzle reflex, menace response, palpebral reflex, and pupillary light reflexes (direct and consensual) were present in both eyes. There was marked left-sided conjunctivitis. Mild aqueous flare was noted within the left anterior chamber. The left iris was swollen and diffusely green/yellow in color, with a 2-mm, pale pink opacity infiltrating the dorso-medial aspect of the iris (Figure 1). In comparison, the right iris was blue in color and aside from mild iris scalloping, no anomalies were noted. Nuclear sclerosis was present bilaterally. No abnormalities were noted on fundic examination in either eye. Both eyes had normal tear production and were fluorescein stain negative. The intraocular pressure in both eyes was within the reference range.

Given the extensive intraocular changes in the left eye, a uveal tumor with secondary iritis and glaucoma was suspected. The differential diagnoses at the time consisted of uveal lymphoma, feline diffuse iris melanoma, traumatic intraocular sarcoma, and ciliary body adenoma/carcinoma. Staging was performed, including 3-view thoracic radiographs and abdominal ultrasound. No anomalies were noted on radiographs and the ultrasound examination revealed 3 hepatic nodules and several splenic nodules. There was no other evidence of metastasis in the imaging performed.

Under general anesthesia, a trans-conjunctival enucleation of the left eye was conducted, along with ultrasound-guided fine-needle aspirates of the hepatic and splenic nodules. The eye was fixed in 10% neutral buffered formalin and embedded in paraffin for histological examination. Cytology from the liver was poorly cellular with a clotted, markedly hemodiluted background and rare ruptured clusters of hepatocytes

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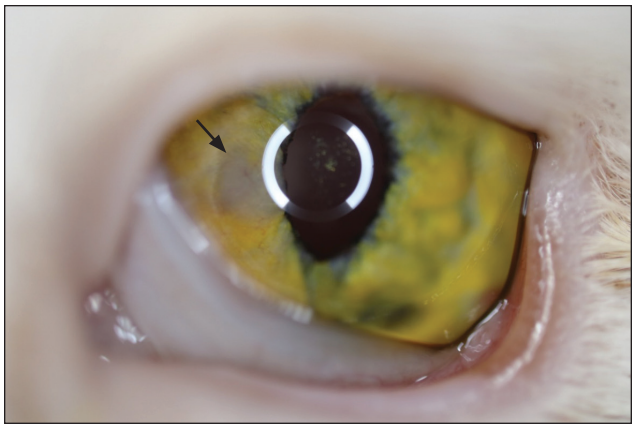

Figure 1. Gross appearance of the left (affected) eye revealing a pale pink-white 2-mm mass (black arrow) and iridal thickening and color change.

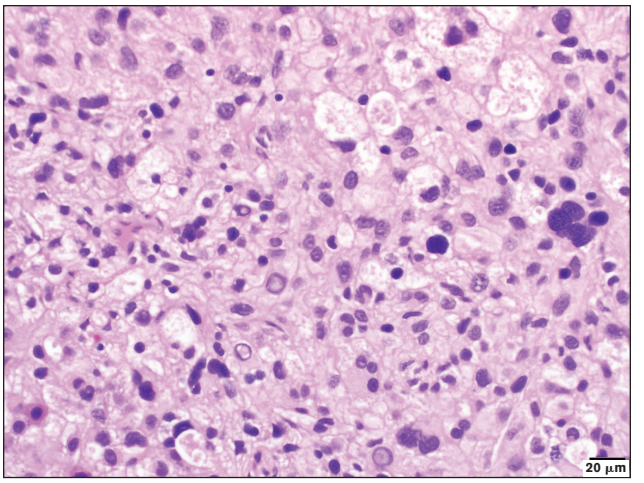

Figure 2. Histology of the uveal tumor consisting of primarily pleomorphic rounds cells with a few spindaloid cells and characterized by marked anisokaryosis, anisocytosis and frequent multinucleated neoplastic cells (Hematoxylin & eosin stain; original magnification 40×).

containing green/black intracytoplasmic pigment (lipofuscin). Similarly, splenic cytology was poorly cellular with a markedly hemodiluted background. There were few individualized small lymphocytes, plasma cells, and well-granulated mast cells. There was no evidence of metastasis in hepatic or splenic cytology; however, both samples were poorly cellular and not necessarily representative.

Histopathology of the left eye revealed an infiltrative neoplasm of the uvea. The neoplasm consisted of primarily pleomorphic round cells as well as a few spindaloid cells with eosinophilic cytoplasm. There was marked anisokaryosis and anisocytosis, with 4 mitotic figures per 10 high power field and frequent bi- and multi-nucleated neoplastic cells (Figure 2). Evidence of mild retinal atrophy and fracturing of the lens, possibly secondary to sectioning, was also noted. Although melanin was not observed within the neoplastic cells, the morphology and location of the cells were highly suggestive of uveal amelanotic melanoma. Immunohistochemistry was recommended to confirm the tentative diagnosis but was declined by the owner.

The cat was discharged with a prescription for a topical tear supplement (Tear Gel; McKesson) 1/4 cm strip, oculus dexter (OD) (right eye), q8h, sub-lingual buprenorphine (Chiron Compounding Pharmacy, Guelph, Ontario), 0.01 mg/kg body weight (BW), PO, q12h, and oral gabapentin (Canadian Pharmaceutical Distribution Network, Toronto, Ontario), 5 mg/kg BW, PO, q12h. The sutures were removed 2 wk after surgery and no anomalies were noted with the surgical site, except for mild swelling. One month after the enucleation, the cat was presented to the OVC-HSC emergency service for constipation, weight loss, and pyrexia, and was diagnosed with a mild diffuse enteropathy and mild mesenteric lymphadenopathy based on abdominal ultrasound. Fine-needle aspirates revealed intestinal small cell lymphoma. Three months following enucleation, there were no concerns with the enucleation site, nor had any melanotic metastases been identified.

Discussion

This case represents an unusual presentation of feline diffuse iris melanoma, as the tumor consisted of an amelanotic mass rather than an area of hyperpigmentation. Although feline malignant melanoma is relatively rare, diffuse iris melanoma is the most common primary feline intraocular tumor (2–5). There is no evidence of breed or sex predisposition, and most cases are detected in middle-aged to older cats (2,4,6). The tumor cells originate on the anterior surface of the iris, and classically are recognized as multifocal or diffuse golden or dark brown-black hyperpigmentation (2,3,7). The lesions may remain unchanged, but in most cases will progress in size, number, and/or thickness over months to years. Dyscoria may be observed due to involvement of the iridal constrictor muscles, and extension into the ciliary body and sclera, or other intraocular structures. Affected cats may be presented with uveitis secondary to tumor promotion of inflammatory mediators, or glaucoma due to infiltration of the iridocorneal angle and obstruction of aqueous outflow. Exfoliation of tumor cells into the aqueous humor or invasion of the tumor into the intraocular vasculature can result in metastasis. A metastatic rate of 16% to 66% has been reported, with the most common sites being the lung and liver, although regional lymph node, splenic, omental, and osseous metastasis have been reported (4,8,9). Metastatic disease may take several years to become clinically apparent, suggesting the need for early recognition and potential enucleation (2). Furthermore, extent of the tumor has a significant impact on survival times, with 1 study showing that invasion of the neoplastic melanocytes into the ciliary body was associated with reduced survival compared to age-matched controls and cats with tumor cells limited to the iris stroma and trabecular meshwork (10). Similarly, patients with secondary glaucoma had a 21% survival rate compared to 73% for those without (10).

The unusual presentation of this case illustrates the importance of including melanoma as a differential diagnosis for non-pigmented or minimally pigmented intraocular neoplasms. As far as the author is aware, this is the first published case of amelanotic uveal melanoma in a cat. A few cases of periocular feline amelanotic melanoma also exist in the literature. Wolfer (11) reported the case of an 8-year-old spayed female domestic short hair cat which was presented for a periocular mass under the

right eyelid. The cytology from fine-needle aspirates of the mass was consistent with a round cell tumor, such as a melanoma or plasmacytoma. A plasmacytoma was ruled out with plasma electrophoresis. In 2006, de Lorimier described a 6.5-year-old spayed female Balinese cat with a large, locally invasive primary orbital melanoma (12). Cytology from a fine-needle aspirate sample revealed spindle-shaped cells with dark cytoplasmic granules consistent with melanoma. Histopathology of the tumor showed atypical cells that appeared highly vacuolated, had poorly defined borders, and contained pleomorphic nuclei consistent with an undifferentiated sarcoma. Immunohistochemistry was needed to confirm the diagnosis of a poorly differentiated, amelanotic melanoma of the orbital tissues (12).

Other intraocular tumors such as uveal lymphoma and feline post-traumatic sarcoma can mimic the gross appearance of amelanotic melanoma and for this reason were considered primary differential diagnoses in the case presented. Lymphoma is one of the most common neoplasms found in cats, with feline uveal lymphoma representing the most frequently observed metastatic uveal tumor (5,13). Intraocular lymphoma is typically assumed to be secondary to systemic multicentric disease. Prognosis is variable, depending on anatomic location and stage of the disease (13). Feline post-traumatic sarcoma is the third most common intraocular neoplasm (14). This tumor has been known to develop several years after trauma to the eye, and can aggressively invade the optic nerve and brain, leading to blindness and other neurologic signs (5,14). Even with prompt enucleation, prognosis is poor due to rapid metastasis (5,14).

Given the differences in treatment and prognosis between the various neoplasms, determining a definitive diagnosis is essential. A study investigating the use of iris biopsy to investigate feline iris hyperpigmentation revealed the potential utility of this diagnostic method in differentiating feline diffuse iris melanoma from benign accumulations of melanocytes; however, at this time iris biopsies are not routinely performed due to perceived risks such as iridal hemorrhage, corneal ulceration, and dyscoria (7).

Currently, histopathology and immunohistochemistry remain the standard of practice in diagnosing intraocular neoplasms. A morphologic diagnosis can often be made based on the microscopic appearance of the cells using hematoxylin & eosin stain. Melanoma is characterized histologically by an accumulation of pleomorphic cells with a variable proportion of round cells, spindle cells, or epithelioid cells (5). The dysplastic melanocytes are often described as plump, with variable anisokaryosis, mitotic index, pigmentation, and nucleoli (6,7). In comparison, intraocular lymphoma appears as infiltrates of neoplastic lymphoid cells within the anterior uvea (5). Similar to amelanotic melanoma, intraocular sarcomas can consist of a variation of spindle cells, epithelioid cells, and round cells (5). In our case, the appearance of the neoplastic cells was diagnostic for a uveal melanoma.

The application of various immunohistochemical labels allows one to distinguish between a variety of tumor types. Immunohistochemistry is especially useful in cases of poorly differentiated tumors, as specific cell markers can help determine the origin and differentiation of these neoplasms when the morphologic diagnosis is uncertain (15). Positive staining for melanocytic markers such as S-100, tyrosinase, and HMSA 5 can help distinguish melanoma from other neoplasms, while expression of LY5 or CD3 antigens is consistent with lymphosarcoma (15). Intraocular sarcomas and metastatic carcinomas are PAS-positive, whereas melanocytic and lymphocytic tumors are negative (15). In a study involving 75 feline globes with intraocular tumors, 8 tumors (10.7%) were reclassified from their original morphologic diagnosis because of their marker expression (15). Similarly, immunohistochemistry allowed for the diagnosis of 5 out of 6 undifferentiated tumors, highlighting the value of immunohistochemical labeling in addition to histopathology. For this reason, immunohistochemistry was recommended in the case presented to confirm the diagnosis of amelanotic diffuse iris melanoma, especially given the lack of pigment within the tumor cells.

In conclusion, amelanotic iris melanoma should be included as a differential diagnosis for any feline intraocular tumor that is poorly pigmented or nonpigmented. As exemplified in this case, histopathology is a necessary diagnostic technique when investigating intraocular neoplasms as gross examination alone can be misleading.

Acknowledgments

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